UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

ILLUMINA, INC.,

Plaintiff,

v.

NATERA, INC.,

Defendant.

Case No. 18-cv-01662-SI

ORDER RE: CLAIM CONSTRUCTION

On January 16, 2019, the Court heard argument on the parties' proposed claim constructions. Having considered the arguments of the parties and the papers submitted, the Court construes the disputed terms as follows.

BACKGROUND

Plaintiff Illumina, Inc. filed this patent infringement suit against defendant Natera, Inc. on March 16, 2018 alleging infringement of U.S. Patent No. 9,493,831 ("the '831 patent") entitled "Methods of fetal abnormality detection." *See* Dkt. No. 1. On August 16, 2018, Natera responded and claimed that it does not infringe the '831 patent and that the '831 patent is invalid. Dkt. No. 61 at 18–20. Natera also counterclaimed against Illumina, alleging infringement of U.S. Patent No. 8,682,592 ("the '592 patent") entitled "System and Method for Cleaning Noisy Genetic Data From Target Individuals Using Genetic Data from Genetically Related Individuals." *Id*. at 20–24.

REQUESTED CONSTRUCTIONS

1. '831 Patent - "selectively enriching a plurality of non-random polynucleotide sequences of genomic DNA from said fetal and maternal cell-free DNA"

The term "selectively enriching a plurality of non-random polynucleotide sequences of

genomic DNA from said fetal and maternal cell-free DNA" is a part of independent claims 1 and 14 of the '831 Patent. In this context, genomic DNA refers to DNA that comes from a fetus' genome. Testing this genomic DNA can reveal genetic traits about the fetus, including whether the fetus is aneuploid.[1] Blood from pregnant females includes both maternal and fetal DNA. Selective enrichment of fetal DNA can increase its concentration in a sample relative to the concentration of the maternal DNA, which makes it possible to test which traits are present in the fetal DNA. By enriching a "non-random polynucleotide sequence," technicians are able to specifically target fetal DNA for enrichment, rather than enriching both the fetal and maternal DNA. Illumina proposes this term be construed as "enriching a plurality of non-random nucleic acid sequences of genomic DNA from a fetal and maternal cell-free DNA sample that meet sequence and/or location criteria selected to facilitate aneuploidy detection." Dkt. No. 69-1. Natera asks the Court to construe the term as "enriching a plurality of selected non-random nucleic acid sequences of genomic DNA from fetal and maternal cell-free DNA." *Id*.

Claim 1, which is representative of claim 14, reads:

> 1. A method for preparing a sequencing library from a maternal blood sample, the method comprising:
>
> a. obtaining a maternal blood sample comprising fetal and maternal cell-free DNA;
>
> b. **selectively enriching a plurality of non-random polynucleotide sequences of genomic DNA from said fetal and maternal cell-free DNA** to generate a library of enriched non-random polynucleotide sequences, wherein said plurality of non-random polynucleotide sequences comprises at least 100 different non-random polynucleotide sequences selected from a chromosome tested for being aneuploid, said enriching comprising:
>
> (i) a first amplification step to generate a plurality of first reaction products, said amplification comprising at least 100 first primers configured to amplify at least 100 different non-random polynucleotide sequences;

[1] Aneuploidy refers to any genetic disorder where there is an abnormal number of chromosomes. The most well-known type of aneuploidy is trisomy-21 which causes Down Syndrome. '831 patent at 13:41–52.

(ii) a second amplification step to generate a second reaction product, said amplification comprising a second set of primers comprising sequences contained in the first reaction products; and

(iii) a third amplification step to generate a third reaction product comprising said library of enriched non-random polynucleotide sequences, said amplification comprising a third set of primers comprising sequences contained in the second reaction products;

wherein at least one primer of at least one of the second and third sets of primers includes a sequence configured to be added to the different non-random polynucleotide sequences to permit the enriched non-random polynucleotide sequences of the library to anneal to a same sequencing primer for the enriched non-random polynucleotide sequences of the library.

'831 Patent at 63:39–64:42.

2. The '592 Patent

The parties dispute the construction of two terms, both of which are part of claim 1. Claim 1 of the '592 patent reads:

1. An ex vivo method for determining a number of copies of a chromosome or chromosome segment of interest in the genome of an individual, the method comprising:

using a single nucleotide polymorphism (SNP) genotyping array or high throughput DNA sequencing to measure genetic material and produce **genetic data for some or all possible alleles** at a plurality of **at least 100 loci on the chromosome or chromosome segment of interest in the individual**, wherein the genetic data is noisy due to a small amount of genetic material from the individual; and wherein the small amount of genetic material from the individual is from fifty or fewer of the individual's cells, 0.3 ng or less of the individual's DNA, extracellular DNA from the individual found in maternal blood, or combinations thereof;

creating a set of one or more hypotheses specifying the number of copies of the chromosome or chromosome segment of interest in the genome of the individual;

determining, on a computer, the probability of each of the hypotheses given the produced genetic data; and

using the probabilities associated with each hypothesis to determine the most likely number of copies of the chromosome or chromosome segment of interest in the genome of the individual.

'592 Patent at 62:39–62.

A. "Genetic data for some or all possible alleles"

The parties dispute the construction of the term "genetic data for some or all possible alleles."[2] Illumina proposes that the term be construed as "data showing the identities of particular bases at specific loci so as to reveal the genotype of the individual for some or all possible alternative forms of the loci." Dkt. No. 70-1 at 3. Natera proposes that the term be construed as "genetic data for some or all possible alternative forms of a given locus." *Id.*

B. "Loci of interest in the individual"

The parties dispute the construction of the term "at least 100 loci on the chromosome or chromosome segment of interest in the individual."[3] Illumina proposes that the Court adopt "as least 100 loci on the chromosome or chromosome segment of interest from only the individual" as the construction. Dkt. No. 70-1 at 1. Natera asserts that no construction is necessary. *Id.*

LEGAL STANDARD

Claim construction is a matter of law. *Markman v. Westview Instr., Inc.*, 517 U.S. 370, 372 (1996). Terms contained in claims are "generally given their ordinary and customary meaning." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005). "[T]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention." *Id.* at 1312. In determining the proper construction of a claim, a court begins with the intrinsic evidence of record, consisting of the claim language, the patent specification, and, if in evidence, the prosecution history. *Id.* at 1313; *see also Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). "The appropriate starting

[2] An allele is particular variation of a gene.

[3] Loci refers to fixed positions within a chromosome. A locus is examined to determine the specific nucleic acid encoded on that part of the chromosome. Examining a number of loci in sequence allows geneticists to determine what variant of a gene, i.e. which allele, an individual has in their genome.

point…is always with the language of the asserted claim itself." *Comark Communications, Inc. v. Harris Corp.*, 156 F.3d 1182, 1186 (Fed. Cir. 1998); *see also Abtox, Inc. v. Exitron Corp.*, 122 F.3d 1019, 1023 (Fed. Cir. 1997).

Accordingly, although claims speak to those skilled in the art, claim terms are construed in light of their ordinary and accustomed meaning, unless examination of the specification, prosecution history, and other claims indicates that the inventor intended otherwise. *See Electro Medical Systems, S.A. v. Cooper Life Sciences, Inc.*, 34 F.3d 1048, 1053 (Fed. Cir. 1994). The written description can provide guidance as to the meaning of the claims, thereby dictating the manner in which the claims are to be construed, even if the guidance is not provided in explicit definitional format. *SciMed Life Systems, Inc. v. Advanced Cardiovascular Systems, Inc.*, 242 F.3d 1337, 1344 (Fed. Cir. 2001). In other words, the specification may define claim terms "by implication" such that the meaning may be "found in or ascertained by a reading of the patent documents." *Vitronics*, 90 F.3d at 1582, 1584 n.6.

In addition, the claims must be read in view of the specification. *Markman v. Westview Instruments*, Inc., 52 F.3d 967, 978 (Fed. Cir. 1995), aff'd, 517 U.S. 370 (1996). Although claims are interpreted in light of the specification, this "does not mean that everything expressed in the specification must be read into all the claims." *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 957 (Fed. Cir. 1983). For instance, limitations from a preferred embodiment described in the specification generally should not be read into the claim language. *See Comark*, 156 F.3d at 1187. However, it is a fundamental rule that "claims must be construed so as to be consistent with the specification." *Phillips*, 415 F.3d at 1316. Therefore, if the specification reveals an intentional disclaimer or disavowal of claim scope, the claims must be read consistently with that limitation. *Id.*

Finally, the Court may consider the prosecution history of the patent, if in evidence. *Markman*, 52 F.3d at 980. The prosecution history limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution. *See Southwall Technologies, Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1576 (Fed. Cir. 1995). In most situations, analysis of this intrinsic evidence alone will resolve claim construction disputes. *See Vitronics*, 90 F.3d at 1583.

Courts should not rely on extrinsic evidence in claim construction to contradict the meaning of claims discernable from examination of the claims, the written description, and the prosecution history. *See Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1308 (Fed. Cir. 1999) (citing *Vitronics*, 90 F.3d at 1583). However, it is entirely appropriate "for a court to consult trustworthy extrinsic evidence to ensure that the claim construction it is tending to from the patent file is not inconsistent with clearly expressed, plainly apposite, and widely held understandings in the pertinent technical field." *Id.* Extrinsic evidence "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Phillips*, 415 F.3d at 1317. All extrinsic evidence should be evaluated in light of the intrinsic evidence. *Id.* at 1319.

DISCUSSION

Pursuant to Patent Local Rule 4-3(a), parties are required to identify up to ten terms whose construction will be most significant to the resolution of the case. Patent L. R. 4-6. The parties have identified three terms for construction in their joint claim construction statements. The Court addresses each of the disputed constructions in turn.

1. '831 Patent - "selectively enriching a plurality of non-random polynucleotide sequences of genomic DNA from said fetal and maternal cell-free DNA[.]"

Term to be construed	Illumina's Construction	Natera's Construction
"selectively enriching a plurality of non-random polynucleotide sequences of genomic DNA from said fetal and maternal cell-free DNA"	enriching a plurality of non-random nucleic acid sequences of genomic DNA from a fetal and maternal cell-free DNA sample that meet sequence and/or location criteria selected to facilitate aneuploidy detection	enriching a plurality of selected non-random nucleic acid sequences of genomic DNA from fetal and maternal cell-free DNA.

Illumina asks the Court to construe the term as one including an aneuploidy detection limitation and asserts the contested term should be construed as "enriching a plurality of non-random

nucleic acid sequences of genomic DNA from a fetal and maternal cell-free DNA sample that meet sequence and/or location criteria selected to facilitate aneuploidy detection." Dkt. No. 71 at 5. Illumina relies on both this Court's prior claim construction in *Verinata Health, Inc., et al. v. Ariosa Diagnostics, Inc., et al.*, 3:12-cv-05501-SI (N.D. Cal.), Dkt. No. 89 (Oct. 16, 2013) and intrinsic evidence within the '831 patent to demonstrate the claim is directed toward aneuploidy detection. Natera counters that the "selected to facilitate aneuploidy detection" limitation should not be in the construction and argues that the intrinsic evidence shows the claims are not limited to aneuploidy detection.

Both Illumina and Natera cite to this Court's prior claim construction in *Verinata*. In that order, the Court construed "selectively" as "criteria selected to facilitate aneuploidy detection" because this limitation was already incorporated into the claim through the preamble and the construction did not limit claim scope. 3:12-cv-05501-SI. (N.D. Cal.), Dkt. No. 89 (Oct. 16, 2013) at 39.

Illumina now argues the Court should adopt its construction because it is "nearly identical" to a construction the Court adopted for a "nearly identical [term]" in *Verinata*. Dkt. No. 71 at 1, 5. *See* Claim Construction Order, *Verinata* at 38–40. Illumina notes that the '831 patent and the '430 patent at issue in *Verinata* stem from the "same parent applications, share identical specifications, and have considerable overlap between their claim language and intrinsic records that justify construing the claim term of the '831 Patent [similarly to the Court's prior construction] for the '430 Patent." Dkt. No. 71 at 1.

Illumina argues this Court's prior '430 patent claim construction demonstrates that the method in the '831 patent contains actual testing for aneuploidy. This Court previously construed the term "reference chromosome" to mean "a chromosome different ***from the particular chromosome that is being tested for aneuploidy***." *Verinata*, Dkt. No. 89 (Oct. 16, 2013) at 43 (emphasis added). Illumina uses this construction to refute Natera's argument that "tested for being aneuploid" merely specifies where the selected sequences come from and not what they are used for. Illumina argues that this Court's prior interpretation indicated the Court interpreted "tested for aneuploid" to mean actual testing for aneuploidy. Accordingly, since both the '831 patent and the

’430 patent contain the identical phrase “chromosome tested for being aneuploid,” Illumina asserts that the same reasoning and conclusion should apply—there is actual testing for aneuploidy that supports Illumina’s construction. Dkt. No. 76 at 3.

Illumina argues that its proposed construction is supported by the patent’s claim language and specification. For example, claim 1 contains the phrase “wherein...at least 100 different non-random polynucleotide sequences selected from a chromosome tested for being aneuploid.” ’831 Patent at 64:48–51; Dkt. No. 71 at 6. Illumina argues this language supports its construction that “selective enrichment” of the claims is carried out to facilitate aneuploid detection and is based on sequence or location criteria. Illumina also points to dependent claims 6 and 13, noting the invention is directed toward a method that involves testing for aneuploidy. Claims 6 and 13 mention “the chromosome tested for being aneuploid” and “said chromosome tested,” respectively. ’831 Patent at 65:8, 27–28. Illumina argues that, “the claims themselves…confirm that selective enrichment is directed towards enriching nucleic acid sequences that are selected to facilitate aneuploidy detection, as recited in Illumina’s proposed construction.” Dkt. No. 71 at 6.

Illumina also points to the specification to support its proposed construction. Specifically, Illumina highlights language in the “Abstract” and “Background of the Invention.” The Abstract states “[m]ethods of using selectively enriched non-random polynucleotide sequences for detection of fetal aneuploidy are provided.” The Background states “[t]here is a need for a means of selectively enriching non-random fetal and maternal polynucleotide sequences in a way that facilitates aneuploidy detection by massively parallel sequencing techniques and increases the sensitivity of aneuploidy detection. . .” ’831 Patent at 1:34–39.

Natera argues that Illumina misapplies the ’430 patent’s claim construction. Dkt. No. 73 at 10–12. Natera points out that there is one important difference between the ’430 patent and ’831 patent at issue: the preamble of the ’430 patent states “determining a presence or absence of a fetal aneuploidy,” while the preamble of the ’831 patent does not mention aneuploidy. Natera argues the ’430 patent claims show Verinata knew how to specify that facilitating aneuploidy detection was the purpose of the claimed invention, and because Verinata failed to include similar limiting language in ’831’s preamble, the claim here should not be limited to aneuploidy detection.

Natera argues that the patent's claim language and specification support its construction. Natera argues that the phrase in claim 1, "tested for being aneuploid…merely specifies where the selected sequences come from—not what they must be used for." Dkt. No. 73 at 9. In addition, Natera argues that the specification does not support Illumina's contention that the invention is directed only toward aneuploidy detection. Natera points out that throughout the specification, aneuploidy analysis is discussed as an exemplary embodiment and not the entire invention, e.g., "[i]n another embodiment, said sequenced enriched sequences are used to determine the presence or absence of fetal aneuploidy." '831 Patent at 3:29–41.

The Court finds that the patent's claim language supports a finding that the '831 is directed to aneuploidy detection. The claim imposes limitations on how non-random sequences are to be selected—that is, they are selected from a chromosome "tested for being aneuploid." This Court's interpretation of that same phrase in the '430 patent demonstrates the claim methods include chromosomes that are actually tested for aneuploidy. Although the preamble of the '831 patent lacks the phrase "determining a presence or absence of fetal aneuploidy," which is present in the '430 patent, the Court finds that the '831 patent is directed to aneuploidy detection. Ultimately, the '831 claims language "tested for being aneuploid" is persuasive in showing the method is directed to aneuploidy detection.

The Court also finds that the specification supports a finding that the '831 patent is directed toward aneuploidy detection. The Abstract and Background state that the invention contains methods for detecting aneuploidy and that there is a need for such detection methods. The fact that the specification frames aneuploidy detection as examples or embodiments is not dispositive and does not overcome the plain language from the Abstract and Background, which inform the bounds of the invention.

For the reasons stated above, the Court to construes "selectively enriching a plurality of non-random polynucleotide sequences of genomic DNA from said fetal and maternal cell-free DNA" to mean: "enriching a plurality of non-random nucleic acid sequences of genomic DNA from a fetal and maternal cell-free DNA sample that meet sequence and/or location criteria selected to facilitate aneuploidy detection."

2. '592 Patent

A. "genetic data for some or all possible alleles"

Term to be construed	Illumina's Construction	Natera's Construction
"genetic data for some or all possible alleles"	data showing the identities of particular bases at specific loci so as to reveal genotype of the individual for some or all possible alternative forms of the loci	genetic data for some or all possible alternative forms of a given locus

The parties dispute whether "genetic data" should be construed broadly as the plain and ordinary meaning of "genetic data" or more narrowly as "data showing the identities of particular bases at specific loci so as to reveal genotype of the individual." Dkt. No. 70-1.

Illumina advocates for a narrow construction, arguing that claim 1 should be limited to genotyping, i.e., "allele-specific" genetic data.[4] Natera argues that claim 1 has a broader scope and should encompass both "allele-specific" and "allele-agnostic" genetic data.[5] Dkt. No. 75 at 4.

Natera supports its broader construction with three main arguments. First, Natera argues that there is a heavy presumption for its construction because it reflects the ordinary and customary meaning. Second, Natera presents examples from the claims and specification of allele-agnostic, i.e., non-genotyping, techniques for measuring genetic data. Third, Natera supports its construction based on a theory of claim differentiation between independent claim 1 and dependent claim 10.

Natera asserts that its broader construction should receive a heavy presumption because it reflects the term's ordinary and customary meaning. Dkt. No. 75 at 6–7. Natera argues that Illumina has not shown "alternative lexicography" or a "clear disavowal" of non-genotyping methods to

[4] An "allele specific" interpretation correlates with "genotyping," "making an allele call," and determining the identification of a base pair at a specific location, or locus, on a chromosome. Dkt. No. 72 at 17. An "allele agnostic" interpretation is not synonymous with any of the terms described above.

[5] Allele-agnostic techniques are techniques that do not require genotyping, i.e., "non-genotyping." In other words, allele-agnostic techniques "ignore the identities of any particular nucleotides at a locus." Dkt. No. 75 at 3.

overcome the presumption. *Id*. at 3, 6.

Natera presents multiple examples of non-genotyping methods from the claim language and specification. In one example, Natera cites to the language of claim 1, "using a [SNP] genotyping array or high throughput DNA sequencing to measure genetic material." '592 patent 62:42–44. Natera argues that this claim language explicitly contemplates both a genotyping technique, "[SNP] genotyping array" and a non-genotyping technique, "high throughput DNA sequencing." Dkt. No. 72 at 13.

Natera also asserts that one "aspect of the invention" is "the direct measurements of the amount of genetic material," which is a non-genotyping technique. Dkt. No. 72 at 14; Dkt. No. 75 at 7–8. Specifically, Natera points to "Sanger DNA sequencing" and "pyrosequencing" from claim 19 and "mini-sequencing…, pyrosequencing…, and genomic sequencing…" from the specification to demonstrate examples of non-genotyping techniques. '592 Patent at 64:5, 3:63, 5:13–14, 8:12; Dkt. No. 72 at 13, 16; Dkt. No. 75 at 8.

Natera finally supports its claim construction under a theory of claim differentiation. Natera argues that dependent claim 10 narrows claim 1, and therefore claim 1 cannot be limited in the way Illumina's construction requires. Dkt. No. 72 at 15. Specifically, Natera asserts that because claim 10 narrows the method to genotyping, claim 1 cannot also have such a narrow interpretation. *Id*.

Illumina supports its narrower construction with three main arguments. First, Illumina argues that "sequencing," in light of the specification, refers only to genotyping and not non-genotyping methods. Second, Illumina asserts that the patentee acted as a lexicographer and limited the claim term "alleles" to genotyping. Third, Illumina asserts that the prosecution history, which only mentions genotyping techniques, should limit the claim scope.

Illumina asserts that the claim language "high throughput DNA sequencing" and "pyrosequencing" must be limited to genotyping. Illumina rejects Natera's assertion that such types of sequencing are examples of non-genotyping techniques. To support this argument, Illumina states that the specification never suggests that "sequencing" is used for anything else but genotyping and SNP determination. Dkt. No. 74 at 20.

Illumina also argues that the patentee acted as its own lexicographer and limited the

definition of "alleles" to genotyping. Dkt. No. 74 at 20–21. Illumina cites the definition section of the specification where "to call an allele" is defined as "to call a SNP." '592 Patent at 62:13. Accordingly, because calling an SNP equates to genotyping, Illumina argues that the term "alleles" must correspond to genotyping. Thus, the claim should be construed as containing a genotyping limitation. Dkt. No. 74 at 20.

Illumina argues that the prosecution history also limits the claim term to genotyping. Dkt. No. 74 at 22–23. Illumina asserts that the only type of techniques disclosed in the 2005 provisional application are based on genotyping. *Id*. at 22. Thus, Illumina argues, the patent should also be limited to only genotyping techniques. *Id*. at 23.

The Court finds that both the claims and specification demonstrate that the claimed method includes both genotyping and non-genotyping techniques. For example, claim 1 states "[SNP] genotyping array or high throughput DNA sequencing." '592 Patent at 62:42–43. This language supports the argument that one disclosed technique is genotyping and the other is non-genotyping. The claims and specification also clearly state that one aspect of the invention is measuring the amount of genetic material, which supports a claim interpretation that includes non-genotyping techniques.

Accordingly, the Court construes the term as it proposed during oral argument, which is with the slight modification construing "genetic data for some or all possible alleles" to mean: "genetic data for some or all possible base pairs at a given locus."

B. "at least 100 loci on the chromosome or chromosome segment of interest in the individual"

Term to be construed	Illumina's Construction	Natera's Construction
"at least 100 loci on the chromosome or chromosome segment of interest in the individual"	at least 100 loci on the chromosome or chromosome segment of interest from only the individual	No construction necessary

The parties dispute the phrase immediately preceding "the individual." Illumina seeks a construction specifying "from only the individual"; Natera seeks to leave the term in its original form, "in the individual." The parties dispute whether, according to the patent claims, an individual's genetic data must be measured separately from the genetic material of another individual, i.e., whether fetal and maternal DNA must be measured separately. Dkt. No. 74 at 10; Dkt. No. 75 at 12.

Natera supports its position with two main arguments. First, Natera points to the technical definition of the claim term "an" to mean more than one. Second, Natera points to "mixed samples" and "foreign DNA" in the specification to argue that the patent is not limited to analyzing an individual's DNA separate from another individual's DNA.

Although the precise claim term being construed is "the individual," Natera argues that the language in the claim's preamble referring to "an individual" supports its construction, since "an" should carry the meaning of "one or more" in open-ended claims that use the transitional phrase, "comprising." Dkt. No. 72 at 18–19, 23. While there is an exception to this rule when "the patentee evinces a clear intent to so limit the article," Natera argues that the exception does not apply here. Dkt. No. 75 at 13; *KCJ Corp. v. Kinetic Concepts, Inc.*, 223 F.3d 1351, 1356 (Fed. Cir. 2000) (the Federal Circuit "has repeatedly emphasized that an indefinite article 'a' or 'an' in patent parlance ***carries the meaning of 'one or more'*** in open-ended claims containing the transitional phrase 'comprising,'"); *Baldwin Graphic Systems, Inc. v. Siebert*, 512 F.3d 1338, 1342 (Fed. Cir. 2008) (The fact that "'a' or 'an' can mean 'one or more' is ***best described as a rule***, rather than merely as a presumption or even a convention.").

Natera also argues that two examples in the specification support its construction. The specification discusses "mixed samples" that contain DNA from multiple individuals and "foreign DNA," which may contaminate the genetic material of an individual being analyzed. *See, e.g.,* '592 Patent at 29:53–57, 40:5–58:54; Dkt. No. 72 at 22– 23. Natera argues that "mixed samples" and "foreign DNA" show that the patent claims are not limited to measuring genetic data for only one individual separately from another individual.

Illumina supports its construction, "…from only the individual," with two main arguments. First, Illumina points to repeated use of "the individual" in the claim language to show that the claims require DNA measurement of only one individual. Second, Illumina cites to the specification that describe isolating fetal DNA from maternal DNA as part of the invention.

Specifically, Illumina highlights the repeated use of the phrase "the individual" to support its construction that the claimed genetic analysis is applied to only one individual separate from another individual. For example, claim 1 states that "the small amount of genetic material ***from the individual*** is from fifty or fewer of ***the individual's cells***, 0.3 ng or less of ***the individual's DNA***, extracellular DNA ***from the individual found in the maternal blood***…" '592 Patent 62:49–52; Dkt. No. 74 at 11. Illumina argues that such language shows that the genetic material of the "individual" is analyzed separately from the DNA of other individuals. Dkt. No. 74 at 11.

Illumina also cites multiple examples in the specification where genetic material, such as "cell-free fetal DNA" is isolated from maternal blood. Dkt. No. 74 at 12–13. Illumina argues that language in the Abstract and Summary of the Invention show that the patent covers reconstructing "noisy" data from the "individual" and cleaning incomplete or noisy genetic data. Dkt. No. 74 at 13. Illumina argues that a prerequisite to these techniques is isolating cells or DNA from a single individual and not from a mixture of multiple individuals. *Id*. at 13–14.

Finally, Illumina rejects Natera's examples of "mixed samples" and "foreign DNA," arguing that the claims "do not cover techniques based on the analysis of truly mixed maternal blood samples that have not been subject to 'isolation' of fetal cells or fetal cell-free DNA." Dkt. No. 74 at 17. Illumina argues that the experiment regarding "mixed samples" is not an embodiment of the patent because it is not limited to "an individual." *Id*. Illumina dismisses the example of a mixed sample as "hypothetical control samples." *Id.* Illumina also states that "nowhere did the experiments assess the number of X chromosomes in the genomes of individuals from whom the mixed samples were prepared." *Id*. Illumina contends that the analysis of foreign DNA

contaminating the sample, which Natera raises, is consistent with Illumina's construction. *Id*.

The Court looks to the language of claims and the specification to determine whether an individual's genetic data must be measured separately from the genetic material of another individual, i.e., whether fetal and maternal DNA must be measured separately. Dkt. No. 74 at 10; Dkt. No. 75 at 12. The Court finds that both the claims and specification demonstrate that the claimed method is directed to the analysis of samples containing the DNA of only one individual. The claim language mentions genetic material from "the individual" many times, often referring to "DNA from the individual *found in maternal blood*." '592 62:52. The claims repeatedly identify the genetic material's source—"the individual"—as distinct from genetic material from another individual, e.g. maternal genetic material. This supports the position that fetal and maternal DNA are measured separately. The specification also repeatedly states that fetal genetic material (e.g. "cell-free fetal DNA") is isolated from the maternal blood prior to analysis. The specification makes clear that the target of analysis is fetal DNA. Accordingly, fetal and maternal DNA are measured separately. Additionally, Illumina stated that the technology for simultaneously analyzing a mixture of maternal and fetal DNA is a "modern approach" that had not yet been invented at the priority date of the '592 patent. Dkt. No. 80 at 112–113.

Accordingly, the Court construes "at least 100 loci on the chromosome or chromosome segment of interest in the individual" to mean: "at least 100 loci on the chromosome or chromosome segment of interest from only the individual."

///

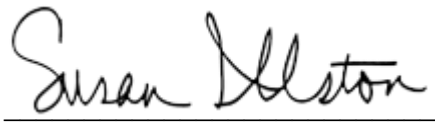
///

CONCLUSION

For the foregoing reasons and for good cause shown, the Court adopts the constructions set forth in this memorandum.

IT IS SO ORDERED.

Dated: January 30, 2019



SUSAN ILLSTON
United States District Judge

United States District Court
Northern District of California